


Racial and ethnic differences in the pharmacologic management of osteoarthritis: rapid systematic review

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Abstract:

Background: Racial and ethnic disparities in osteoarthritis (OA) patients' disease experience may be related to marked differences in the utilization and prescription of pharmacologic treatments.

Objectives: The main objective of this rapid systematic review was to evaluate studies that examined race/ethnic differences in the use of pharmacologic treatments for OA.

Data sources and methods: A literature search (PubMed and Embase) was ran on 25 February 2022. Studies that evaluated race/ethnic differences in the use of OA pharmacologic treatments were included. Two reviewers independently screened titles and abstracts and abstracted data from full-text articles. Preferred Reporting Items of Systematic Reviews and Meta-Analyses (PRISMA) guidelines were followed.

Results: The search yielded 3880 titles, and 17 studies were included in this review. African Americans and Hispanics were more likely than non-Hispanic Whites to use prescription non-selective non-steroidal anti-inflammatory drugs (NSAIDs) for OA. However, compared to non-Hispanic Whites with OA, African Americans and Hispanics with OA were less likely to receive a prescription for cyclooxygenase-2-selective NSAIDs and less likely to report the use of joint health supplements (i.e. glucosamine and chondroitin sulfate). There were minimal/no significant race/ethnic differences in the patient-reported use of the following OA therapies: acetaminophen, opioids, and other complementary/alternative medicines (vitamins, minerals, and herbs). There were also no significant race differences in the receipt of intra-articular therapies (i.e. glucocorticoid or hyaluronic acid). However, there is limited evidence to suggest that African Americans may be less likely than Whites to receive opioids and intra-articular therapies in some OA patient populations.

Conclusion: This systematic review provides an overview of the current pharmacologic options for OA, with a focus on race and ethnic differences in the use of such medical therapies.

Keywords: African Americans, ethnicity, Hispanics, medications, osteoarthritis, race, utilization

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Introduction

The prevalence of osteoarthritis (OA) is significantly higher in African Americans (AAs) than in non-Hispanic Whites (WHs).^{1–3} The exact prevalence of OA in Hispanics (HISs) is unknown, but there are estimates that 12–22% of HISs have arthritis, of which OA is the most common type.⁴ In one study cohort, the

prevalence of radiographic knee OA was highest among AAs compared to WHs and HISs (52.4%, 36.2%, and 37.6%, respectively).⁵ According to a national survey, the prevalence of activity limitation, work limitation, and severe joint pain is also significantly higher among AAs and HISs than among WHs.⁶ Other studies on racial or ethnic disparities in self-reported pain and

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function among OA patients have also shown that racial or ethnic minority status is associated with greater experience of OA-related symptoms and higher prevalence of OA risk factors.⁷⁻⁹

The American College of Rheumatology (ACR) and the Arthritis Foundation (AF), and the Osteoarthritis Research Society International (OARSI) have updated recommendations for the management of knee, hip, and hand OA.^{10,11} Both of these guidelines recommend the use of medications, such as acetaminophen and non-steroidal anti-inflammatory drugs (NSAIDs), when indicated. They report good evidence for the use of topical therapies (e.g. capsaicin and diclofenac) in managing certain types of OA. The use of intra-articular corticosteroid injection is endorsed by both guidelines.^{10,11} The use of intra-articular hyaluronic acid injection for OA is controversial, however. Opioids are generally not recommended, except when more conservative therapies have failed. Most complementary and alternative medicines (CAMs) are also not recommended.

Racial or ethnic disparities in patients' experience of pain may in part be related to marked differences in the use and prescription receipt of OA medical treatments. Several studies have suggested that there are likely race and ethnic differences in the use of pharmacologic treatments that may be used by patients with OA in the United States.¹²⁻¹⁶ In a national survey, AAs and HISs were found to be less likely than WHs to regularly use NSAIDs from 1988 to 1994 and from 1999 to 2004.¹² Among Medicaid recipients, the odds of receiving a prescription for a cyclooxygenase-2 (COX-2)-selective (instead of a non-selective) NSAID were three times lower among AAs and other races compared to WHs.¹³ Data from the National Hospital Ambulatory Medical Care Surveys also showed that AAs and HISs were less likely than WHs to receive an opioid analgesic in the emergency room.¹⁴ There is also evidence to suggest that AAs and HISs are less likely to use different types of CAMs for various conditions.^{15,16} The patients' diagnoses in these studies¹²⁻¹⁶ were not limited to patients with OA, however, and as such may not be generalizable to patients with OA as these therapies are often used to also treat other conditions that can cause acute or chronic pain.

A recent narrative review by Reyes and Katz¹⁷ reviewed the literature on racial and socioeconomic disparities in the management of OA.

Treatments that were investigated included non-pharmacologic, surgical, and pharmacologic agents. They concluded that AAs and HISs, compared to WHs, were more likely to get non-selective NSAIDs rather than COX-2-selective NSAIDs and were less likely to receive opioid medications. However, a systematic review was not done. The review did not provide a comprehensive literature search of studies that evaluated racial/ethnic differences in pharmacologic treatments for OA. It provided minimal information on the quality of the studies that were referenced. It also provided no information on the effects of sociodemographic and clinic factors on observed racial/ethnic differences in OA treatments. A systematic review can help address these limitations.¹⁸

Previously published systematic reviews had provided some insight on the intersection of race/ethnicity, OA, and pharmacologic treatment use. A review by Vaughn *et al.*¹⁹ found higher pain severity and functional disability due to OA among AAs compared to WHs, but the study did not examine racial differences in OA treatment use that could affect these OA symptoms. Other systematic reviews concluded that AAs were less likely than WHs to receive opioid analgesics, especially for non-traumatic or non-surgical pain in the United States.^{20,21} However, these reviews did not exclusively study those with OA and primarily focused on the use of opioid treatments. Other studies performed systematic reviews to identify the role and efficacy of analgesics and other pharmacologic treatments for OA.²²⁻²⁴ They found that the use of non-selective NSAIDs, COX-2 inhibitors, and opioids had similar effects, but none of the studies examined racial/ethnic differences in the actual use of these treatments.

The primary objective of this rapid systematic review was to examine race/ethnic differences in the use of pharmacologic treatments for OA. The secondary objective was to determine the extent of evidence for race/ethnic differences in OA treatment use when adjusted for sociodemographic and clinical factors.

Methodology

The study was performed, and the findings were reported following the Preferred Reporting Items of Systematic Reviews and Meta-Analyses (PRISMA) guidelines.²⁵ The study was not registered with the International Prospective Register of Systematic Reviews; this will be done in future studies.

Search terms and database

To identify studies to include or consider for this rapid review, the review team worked with a medical librarian (SR) to develop detailed search strategies for each database. The searches were conducted following the PRISMA-S extension for search reporting. The medical librarian developed the search for PubMed (National Library of Medicine, NLM) and translated the search for every database searched. The PubMed search strategy was reviewed by the research team to check for accuracy and term relevancy. The Hispanic/Latinx search hedge used in this search was borrowed from the Medical Library Association (MLA) Latinx Search Hedge.²⁶ The databases included in this search are PubMed (NLM) and Embase (Elsevier) using a combination of keywords and subject headings. All final searches were performed on 25 February 2022 by the librarian. The full search strategies as reported by the librarian are provided in Supplement 1.

Study selection

Studies were screened by title and abstract by two blinded and independent reviewers [EV and PH (or SA)]. If a tiebreaker was needed, a third reviewer (NM) was called in. Rayyan (<https://www.rayyan.ai>), a free web app, was used to help expedite the process of screening and selecting studies. Upon instances when inadequate information was available (e.g. full text was unavailable), primary investigators were contacted by e-mail for additional information.

We searched the literature for studies that included human study participants with any type of OA (e.g. knee, hip, or hand OA). We focused on studies that evaluated race/ethnic differences in the use or the receipt of prescriptions for any of the following pharmacologic treatments for OA: acetaminophen; oral non-selective NSAIDs, COX-2-selective NSAIDs; opioids, including tramadol; intra-articular therapies, such as glucocorticoids and hyaluronic acid; topical therapies; and CAMs (specifically, joint health supplements, vitamins/minerals, and herbs). We excluded non-full-text, English-language articles. Case reports, case series studies, conference abstracts/proceedings, and narrative literature reviews were excluded as well as studies that primarily evaluated non-human subjects. Studies that did not evaluate specific pharmacologic treatment use/prescription for OA and those that did not assess OA treatment use by race/ethnicity were also excluded.

Data extraction

Full-text articles were reviewed, and data were abstracted by two independent reviewers [NM and PH (or SA)]. If a tiebreaker was needed, a third reviewer (EV) was used to review the full-text article. The following data were abstracted: data source; specific pharmacologic (traditional and complementary/alternative) OA treatment/s evaluated; study population characteristics [geographic location, community sample *vs* veterans, mean age, gender, race (AA, WH, or others), ethnicity (Hispanic or non-Hispanic)]; percentage of reported study participants who utilized each pharmacologic treatment by race; and variables (sociodemographic and clinical) race/ethnic differences in treatment utilization were adjusted for. To evaluate for variables that could affect the risk of bias in the included studies, the following were also determined: sample size (by race/ethnicity); method in which race/ethnicity information was measured (patient/study participant self-report *vs* physician report *vs* medical record information); study design and study time period; and pharmacologic treatment utilization measure (patient-reported survey *vs* pharmacy database report). Relevant characteristics of all studies included were tabulated.

In addition, we examined whether there were significant race/ethnic differences in treatment utilization of each pharmacologic treatment (i.e. study outcomes) based on each study's reported results. We also determined if the associations were based on bivariate or multivariate analyses. Such information were tabulated and organized by OA pharmacologic treatment type. The studies and the relevant data were presented descriptively and similarly organized in the Results section. ERV and AHR participated in qualitatively synthesizing the reported study results related to the outcomes of interest.

Results

The search resulted in 3880 studies, and 331 duplicate studies were found and omitted by the librarian. Two additional article were identified from review of the papers. There was minimal disagreement (1.9% of records screened) between the two authors who initially screened the study titles and abstracts for potential study inclusion. Seventy-six articles that potentially met the inclusion and exclusion criteria were identified from the title and abstract review. Twenty-one articles met the inclusion and exclusion criteria after

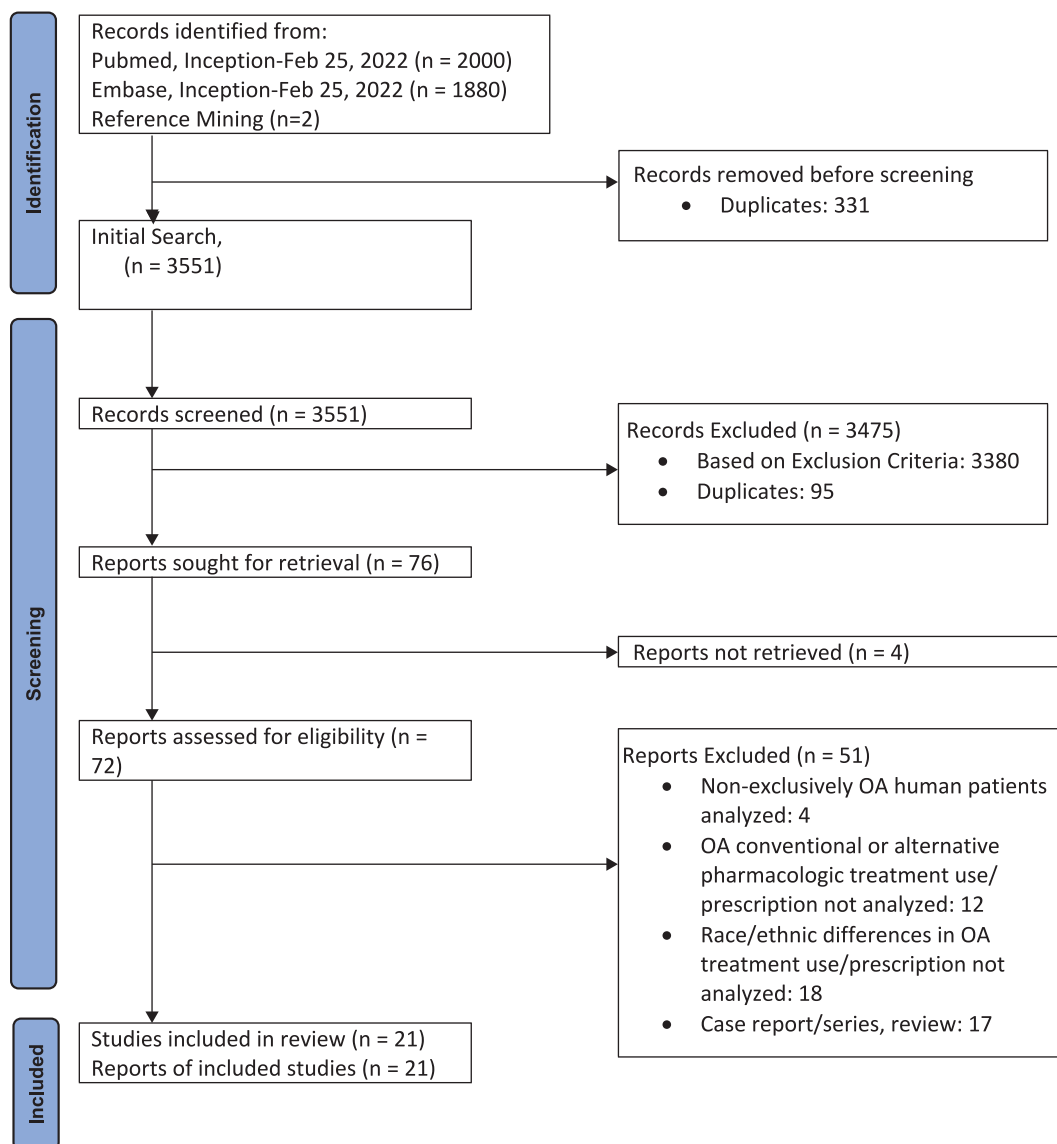


Figure 1. Flow diagram.

full-text review. The article flow (Figure 1) summarizes our study identification and selection.

Study characteristics

There were different ways in which OA patients were identified in the studies. Many (7 studies) used International Classification of Disease–9 diagnosis codes.^{27–33} Others (8 studies) used self-report questionnaires such as The National Health and Nutrition Examination Survey criteria.^{34–41} Table 1 summarizes the clinical setting, the characteristics of the sample population, and the pharmacologic treatment utilization measure of all studies included ($n = 21$). All studies were done in the United States. Community samples were generally studied, but six studies focused on

US veterans. OA treatment utilization was compared between AAs and WHs in 14 studies, between HISs and non-HISs (mostly WHs) in eight studies, between Asian-Americans and other races in two studies, and between ‘non-WHs’ and WHs in three studies. Half of the studies measured race and/or ethnicity based on study participant self-report, but the other half based the information on medical records. Information on OA treatment utilization gathered were based on surveys of study participants in 16 studies, but five were based on evaluating pharmacy databases. Most study designs were cross-sectional in nature (17 out of 21), and four were cohort studies. Most of the studies evaluated race/ethnic differences in pharmacologic treatment use adjusted for sociodemographic and clinical characteristics

(Tables 2–5). However, a few evaluations were unadjusted for these variables (2 NSAID, 4 opioid, 2 acetaminophen, 1 intra-articular therapy, and 3 CAM use studies).^{34,37,39,40,42}

Oral NSAIDs

There has been a proliferation of studies that investigated race/ethnic differences in the use of oral NSAIDs among those with OA in the last two decades (Table 2). In several studies, non-selective were differentiated from COX-2 selective NSAIDs.^{30–32,36,39,40} Some studies also differentiated between prescribed *versus* over-the-counter NSAID use.^{38–40}

Non-selective NSAIDs. Several studies found that prescription non-selective NSAIDs were more often used by AAs than WHs.^{28,31,32,39} The studies were done in various geographic regions of the United States and had large sample sizes (Table 2). Dominick *et al.*³¹ evaluated prescription-use data among those who had a physician visit in North Carolina ($n=2473$). They found that AAs with OA were more likely to receive a prescription for non-selective NSAIDs than WHs with OA. They also conducted a similar evaluation using outpatient prescription data from a national Veterans Affairs (VA) database ($n=4287$) and found similar results.³² These study findings were replicated by Yang *et al.*³⁹ based on data of more than 2500 study participants from the Osteoarthritis Initiative (OAI), a multi-center longitudinal cohort study. A few OAI studies also found that non-WHs (including AAs) were more likely than WHs to report using over-the-counter non-selective NSAIDs.^{39,40} Furthermore, the observed racial/ethnic differences in the use of non-selective NSAID persisted after adjustment for sociodemographic and clinical characteristics.^{28,31,32}

However, in a large administrative data survey, this race difference in the use of NSAIDs was found only in one study time period (1992–1994) but not others.²⁸ In a survey of Medicare beneficiaries who resided in Pennsylvania ($n=551$), the opposite was found.³⁶ Upon review of their prescription medicines, AAs were less likely to have a prescription for non-selective NSAIDs than WHs. Studies with relatively small samples also showed no race differences in the use of non-selective NSAIDs.^{30,43} Upon evaluating the self-reported use of non-selective NSAIDs among >200 OA patients from North Carolina, Dominick *et al.*³⁰ found minimal racial difference in the use of prescription and

over-the-counter NSAIDs. Another study that included clinical trial study participants living in North Carolina ($n=1187$) also concluded that race was not associated with the self-reported use of NSAIDs.⁴³

Very few studies have evaluated differences in the use of NSAIDs between HISs and non-Hispanics.^{27,32,38} Vina *et al.*³⁸ surveyed >300 HISs and non-Hispanic WHs with knee or hip OA living in Arizona. The investigators found that HISs were more likely than non-Hispanic WHs to use prescription NSAIDs. They found that HISs were less likely than non-Hispanic WHs to use over-the-counter NSAIDs, however. Dominick *et al.*'s³² study of prescription data from a national VA database found similar results. The ethnic difference in the use of NSAIDs persisted after adjustment for sociodemographic and clinical characteristics in Dominick *et al.*'s³² study but not in the other studies.^{27,38}

COX-2-selective NSAIDs. In contrast, several of the same studies found that COX-2-selective NSAIDs were less often used by AAs than WHs (Table 2).^{31,32,39,40} Again, the studies had relatively large sample sizes and were conducted in various parts of the United States (Table 2). In the evaluation of VA prescription data in North Carolina³¹ and other regions nationwide ($n=4287$),³² AAs with OA were consistently less likely to receive a prescription for COX-2-selective NSAIDs than WHs with OA. The observed race differences also persisted after controlling for various sociodemographic and clinical factors.^{31,32} Similarly, AAs with knee OA were less likely to report having a prescription for COX-2 inhibitors than WHs with knee OA in OAI studies.^{39,40}

Other studies found no race differences in the use of COX-2-selective NSAIDs for OA, however.^{30,36,44} In a study of people with self-reported arthritis living in Alabama ($n=1380$), a quarter of AAs and a quarter of WHs reported current use of a COX-2-specific NSAID.⁴⁴ In Dominick *et al.*'s³⁰ survey of more than 200 veterans receiving OA care, there was also no significant race difference in the patient-reported use of COX-2 inhibitor agents. Study investigators who examined the use of arthritis-specific medications among Medicare beneficiaries living in Pennsylvania found similar results.³⁶

Opioids

Most survey studies found no race differences in the use of opioids among those with OA.^{30,36,39,40,42–44}

These particular studies were done in various parts of the United States and included those with relatively small and large sample sizes (Table 3). In Mikuls *et al.*'s⁴⁴ study of community-dwelling older adults with arthritis who resided in Alabama, AAs and WHs were equally likely to report using a prescription opioid analgesic (~<5%). While AAs were slightly less likely to report using opioids for arthritis than WHs among veterans in a small study sample ($n=202$) in North Carolina, the investigators found no statistically significant difference when comparing the two race groups.³⁰ A study of other OA cohorts from the same geographical region reported similar results.⁴³ In both the study of Medicare beneficiaries living in Pennsylvania ($n=551$) and the OAI study ($n=2583$) that included study participants from different Midwest and Northeast regions of the United States, no race differences in the use of opioids for OA were found.^{36,39} A similar observation was also found when only OAI study participants with radiographic evidence of knee OA were evaluated.⁴⁰ Similarly, the Arizona study found no difference in the use of opioids for knee/hip OA between HISs and non-Hispanic WHs.³⁷

Analyses of prescription records from the Department of VA administrative database had different results, however.^{29,31} In the study of patients treated at the Durham (North Carolina) VA Medical Center ($n=2479$), AAs were less likely to be prescribed an opioid compared to WHs.²⁹ A single analysis of a national survey ($n=2139$) found that AAs had a higher likelihood of receiving an opioid prescribed by primary-care providers than WHs; this observation was no longer significant when adjusted for various patient- (age, sex, ethnicity, and insurance), clinical- (physical therapy referral, counseling, radiograph findings, and visit type), physician- (primary care access, other provider access, and full/part-time), and practice- (solo, clinic ownership, rural, and region) related characteristics, however.²⁷

Acetaminophen

More than a few studies have examined race differences in the use of acetaminophen for OA (Table 4).^{28,30,31,39,40} Dominick *et al.*'s³¹ study of VA prescription data among veterans in North Carolina found no difference in the prescription of acetaminophen between AAs and WHs with OA. A survey of prescription receipt of knee OA patients nationwide ($n=1728$) yielded the same result.²⁸ The survey of OAI study participants yielded a different

finding, however. Acetaminophen use was more commonly reported by AAs than WHs among OAI participants with radiographic knee OA.³⁹ Similarly, a survey of only those with radiographic knee OA found that non-WHs were more likely than WHs to be using acetaminophen.⁴⁰

Intra-articular therapies

A few studies have investigated potential race differences in the use of intra-articular therapies among those with OA (Table 4).^{33,39,41,43} AA OAI study participants were as likely as WH OAI study participants to report receiving intra-articular glucocorticoid and hyaluronic acid knee injections for joint pain or arthritis in the past 30 days.³⁹ Similarly, Abbate *et al.*'s⁴³ study of OA clinical trial participants living in North Carolina found that intra-articular knee injection use did not differ between AAs and WHs. However, upon evaluating OAI study participants with knee OA who had received at least one joint injection exclusively, AAs were found to be less likely than WHs to report receipt of either glucocorticoid or hyaluronic acid joint injection.⁴¹ In addition, a study of knee or hip OA patients in a tertiary center in North Carolina found that AAs were likely than WHs to receive an intra-articular knee, but not hip, joint injection.³³ Race differences persisted after adjustment for patient sociodemographic characteristics in both studies.^{33,41}

Topical therapies

Although several OA studies evaluated potential race differences in the use of topical therapies,^{36,43,45,46} the specific topical therapies [NSAIDs, capsaicin, lidocaine, CAM-based therapies (herbal, oils/lotions)] were typically not differentiated from one another,^{36,43} except for two studies.^{45,47} Herman *et al.*'s⁴⁷ study in New Mexico ($n=422$) found that there were no significant differences between HISs and WHs in the use of topical herbal rubs. Katz and Lee's⁴⁵ study of clinical trial participants from various states ($n=859$) found that AAs (42.9%) and HISs (38.6%) were more likely to use CAM-based topical agents than WHs (30.5%).

CAMs

Most studies found that racial and ethnic minorities were less likely to be using glucosamine and chondroitin sulfate than non-Hispanic WHs (Table 5).^{39,40,44,45,47,48} AAs were less likely than WHs to report use of these joint health

Table 1. Basic characteristics of studies included.

Investigator(s)	Geographic location	Study population	Mean Age (years)	Sex (%female)	# Study participants by race/ethnicity	Race/ethnicity measure	Utilization measure	Study design (study time period)
Coulton <i>et al.</i> ³⁴	Ohio	Community sample	~72	~70	WH (112), AA (105), HIS (100)	Self-report	Survey	Cross-sectional (N/A)
Ausiello and Stafford ²⁸	All states in the USA	Community sample	N/A	68.8	WH (1433), Non-WH (295)	Physician report or medical record	Survey	Cohort (1989–1991, 1992–1994, 1995–1998)
Mikulski <i>et al.</i> ⁴⁴	Alabama	Community sample	~65	~72	WH (852), AA (528)	Self-report	Survey	Cross-sectional (2001)
Dominick <i>et al.</i> ³¹	North Carolina	Veterans	61	5	WH (1612), AA (861)	Medical record	Pharmacy database	Cross-sectional (1998–1999)
Dominick <i>et al.</i> ³²	All states in the USA	Veterans	61	5	WH (3410), AA (686), HIS (191)	Medical record	Pharmacy database	Cohort (2000)
Dominick <i>et al.</i> ³⁰	North Carolina	Veterans	64	9	WH (141), AA (61)	Medical record	Survey	Cross-sectional (2002–2003)
Dominick <i>et al.</i> ²⁹	North Carolina	Veterans	60	4	WH (1622), AA (857)	Medical record	Pharmacy database	Cross-sectional (1998–1999)
Herman <i>et al.</i> ⁴⁷	New Mexico	Community sample	N/A	67	WH (204), HIS (218)	Medical record	Survey	Cross-sectional (2000–2001)
Katz and Lee ⁴⁵	Multiple states in the USA	Community sample	61	68	WH (220), AA (322), HIS (317)	Self-report	Survey	Cross-sectional data from randomized controlled trials (N/A)
Albert <i>et al.</i> ³⁶	Pennsylvania	Community sample	~73	~60	WH (267), AA (284)	Self-report	Survey	Cross-sectional (2001–2002)
Marcum <i>et al.</i> ³⁵	Pennsylvania, Tennessee	Community sample	79	66	WH (390), AA (262)	Self-report	Survey	Cross-sectional (2002–2003)
Yang <i>et al.</i> ³⁹	Multiple states in the USA: Maryland, Ohio, Pennsylvania, and Rhode Island	Community sample	>65	~63	WH (2075), AA (508)	Self-report	Survey	Cross-sectional data from cohort study (2004–2006)

(Continued)

Table 1. (Continued)

Investigator(s)	Geographic location	Study population	Mean Age (years)	Sex (%female)	# Study participants by race/ethnicity	Race/ethnicity measure	Utilization measure	Study design (study time period)
Kingsbury <i>et al.</i> ⁴⁰	Multiple states in the USA: Maryland, Ohio, Pennsylvania, and Rhode Island	Community sample	~62	~56	WH(701), Non-WH (286)	Self-report	Survey	Cohort (N/A)
Lapane <i>et al.</i> ⁴¹	Multiple states in the USA: Maryland, Ohio, Pennsylvania, and Rhode Island	Community Sample	~65	~58	WH (1,757), AA (~429), Other (~71)	Self-report	Survey	Cross-sectional data from cohort study (2004–2006)
Abbate <i>et al.</i> ⁴³	North Carolina	Community sample and veterans	~63	~52	WH (723), Non-WH (464)	Unknown	Survey	Cross-sectional data from randomized controlled trials (N/A)
Consson <i>et al.</i> ⁴²	Northwest USA	Community sample	~66	~58	WH (573), HIS Non-WH (48)	Medical record	Pharmacy database	Cohort (2016–2017)
Vina <i>et al.</i> ³⁸	Arizona	Community sample	~63	~71	WH (204), HIS (130)	Self-report	Survey	Cross-sectional (2015–2018)
Khoja <i>et al.</i> ²⁷	All states in the USA	Community Sample	64	~64	WH (1902), AA (237).	Physician report or medical record	Survey	Cross-sectional (2007–2015)
Vina <i>et al.</i> ³⁷	Arizona	Community sample	~64	70	Non-HIS (228), HIS (121)	Self-report	Survey	Cross-sectional (2015–2018)
Vina <i>et al.</i> ⁴⁸	Pennsylvania	Veterans	64	27	WH (247), AA (270)	Self-report	Survey	Cross-sectional data from randomized controlled trial (2018)
Wu <i>et al.</i> ³³	North Carolina	Community sample	N/A	N/A	WH(74769), AA (27117), HIS (14779), Asians (1479)	Medical record	Pharmacy database	Cohort (2013–2020)

AA, African-American; HIS, Hispanic; WH, White.

Table 2. Studies that investigated race/ethnic differences in the use of non-steroidal anti-inflammatory drugs (NSAIDs) for OA.

Investigator(s)	Findings	Variables adjusted for	Findings after adjustment
Ausiello and Stafford ²⁸	NS: Non-WHs (50.9%) \approx WHs (45.1%), 1989–1991. NS: Non-WHs (48.9%) > WHs (38.7%), 1992–1994. NS: Non-WHs (36.5%) \approx WHs (31.7%), 1995–1998.	Age, sex, patient insurance, and physician specialty	Race difference in 1992–1994 persisted. Lack of association in other years (1989–1991, 1995–1998) persisted.
Mikulski <i>et al.</i> ⁴⁴	COX-2: \sim 25% AAs \approx \sim 25% WHs	Marital status, education, joint swelling/stiffness, and rheumatoid arthritis diagnosis	Lack of association persisted
Dominick <i>et al.</i> ³¹	COX-2: AAs (4.1%) < WHs (7.4%) Prescription NS: AAs (69.1%) > WHs (60.3%)	Age, sex, service connection, and having arthroplasty (5 years)	Race differences persisted
Dominick <i>et al.</i> ³²	COX-2: AAs (8.9%), HISs (7.3%) < WHs (10.2%) Prescription NS: AAs (86.4%), (HISs 79.0%) > WHs (73.1%)	Age, sex, geographic location, comorbidities, history of GI bleed, use of anticoagulants, and use of corticosteroids	COX-2: Ethnic difference persisted, but race difference ($p=0.028$) did “not”
Dominick <i>et al.</i> ³⁰	COX-2: AAs (13.1%) \approx WHs (18.4%) NS: AAs (50.8%) \approx WHs (46.1%)	Age, gender, education, WOMAC, years with OA, and number of affected joints	Lack of associations persisted
Albert <i>et al.</i> ³⁶	COX-2: AAs (9.7–29.5%) \approx WHs (20.0–34.4%) Prescription NS: AAs (22.6–29.0%) < WHs (35.8–42.6%)	Gender, severity of arthritis, age, education, pain, and access to prescription	COX-2: Race difference did not persist NS: Race difference persisted
Yang <i>et al.</i> ³⁹	COX-2: AAs (5.7%) < WHs (9.3%) Over-the-counter NS: AAs (28.0%) > WHs (19.5%); Prescription NS: AAs (10.2%) > WHs (7.0%)	Unadjusted	N/A
Kingsbury <i>et al.</i> ⁴⁰	COX-2: Non-WHs (6.6%) < WHs (11.7%) Over-the-counter NS: Non-WHs (32.3%) > WHs (24.7%) Prescription NS: Non-WHs (8.7) \approx WHs (8.0%)	Unadjusted	N/A
Abbate <i>et al.</i> ⁴³	NS: Non-WH race not associated with NS use (multivariable-adjusted model)	Age, sex, income, health, body mass index, WOMAC, OA symptoms, and knee/hip OA	Lack of associations persisted
Vina <i>et al.</i> ³⁸	Over-the-counter NS: HISs (52.9%) < WHs (66.3%) Prescription NS: HISs (43.4%) > WHs (31.7%)	Age, sex, education, and private medical insurance	Ethnic differences did not persist
Khoja <i>et al.</i> ²⁷	AA race not associated with NS prescription. HIS ethnicity associated with > likelihood of NS prescription (by orthopedists)	Clinical characteristics, patient demographics, physician characteristics, and practice characteristics	Ethnic difference in NS prescription (by orthopedists) did not persist

AA, African-American; COX-2, cyclooxygenase-2 selective NSAID; GI, gastrointestinal; HIS, Hispanic; NS, non-selective (not cyclooxygenase-2 selective) NSAID; NSAIDs, non-steroidal anti-inflammatory drugs; OA, osteoarthritis; WH, White; WOMAC, Western Ontario and McMaster Universities Osteoarthritis Index.

Table 3. Studies that investigated race/ethnic differences in the use of opioids for OA.

Investigator(s)	Findings	Variables adjusted for	Findings after adjustment
Mikul's <i>et al.</i> ⁴⁴	AAs (~5%) ≈ WHs (~5%)	Gender, education, joint swelling, comorbidity, rural residence, and income	Lack of association persisted
Dominick <i>et al.</i> ³¹	AAs (32.6%) < WHs (40.1%)	Age, sex, service connection, having arthroplasty (5 years)	Race difference persisted
Dominick <i>et al.</i> ³⁰	AAs (14.8%) ≈ WHs (21.3%)	Age, gender, education, WOMAC, years with OA, and number of affected joints	Lack of association persisted
Dominick <i>et al.</i> ²⁹	AAs (39.0%) < WHs (47.3%)	Gender and service connection	Race difference persisted
Albert <i>et al.</i> ³⁶	AAs (3.2–17%) ≈ WHs (6.2–14.5%)	Gender and severity of arthritis (stratified only)	N/A
Marcum <i>et al.</i> ³⁵	AA race not associated with opioid use	OA pain severity, age, sex, site, education, osteoporosis, health status factors (osteoporosis and cancer), health, body mass index, and access to healthcare	Lack of association persisted
Yang <i>et al.</i> ³⁹	AAs (3.9%) ≈ WHs (2.6%)	Unadjusted	N/A
Kingsbury <i>et al.</i> ⁴⁰	Non-WHs (4.9%) ≈ WHs (2.7%)	Unadjusted	N/A
Consson <i>et al.</i> ⁴²	HIS non-WHs (27.1%) ≈ WHs (27.6%)	Unadjusted	N/A
Vina <i>et al.</i> ³⁷	HISs (30.5%) ≈ non-HISs (27.5%)	Unadjusted	N/A
Khoja <i>et al.</i> ²⁷	AA race associated with > likelihood of opioid prescription (by primary care physician). HIS race not associated with opioid prescription.	Clinical characteristics, patient demographics, physician characteristics, and practice characteristics	Race difference in opioid prescription (by primary care physician) did not persist

AA, African-American; HIS, Hispanic; OA, osteoarthritis; WH, White; WOMAC, Western Ontario and McMaster Universities Osteoarthritis Index.

supplements among a sample of Alabamans with OA by Mikul's *et al.*,⁴⁴ among AA and WH OAI study participants by Yang *et al.*³⁹ and among veterans who participated in a clinical trial by Vina *et al.*⁴⁸ Similarly, HISs were less likely than WHs to report use of these supplements among Herman *et al.*'s⁴⁷ sample of New Mexicans with OA. Kingsbury *et al.*'s⁴⁰ comparison between non-WHs and WHs among OAI study participants with radiographic knee OA found similar results.

Nearly all studies that investigated the use of vitamins and minerals for OA found that there were minimal race and ethnic differences in the patient-reported use of these supplements (Table 4).^{34,39,47,48} An exception was Katz and Lee's⁴⁵ multi-state/multi-center investigation of clinical trial study participants. In this investigation, AAs and HISs were more likely than WHs to report use of vitamins or minerals to help with their arthritis. Race difference in any CAM use (not just vitamins/minerals) per-

Table 4. Studies that investigated race/ethnic differences in the use of other conventional therapies for OA.

Investigator(s)	Findings	Variables adjusted for	Findings after adjustment
Ausiello and Stafford ²⁸	ACE: Non-WHs (2.7%) ≈ WHs (5.1%), 1989–1991. ACE: Non-WHs (8.3%) ≈ WHs (7.6%), 1992–1994. ACE: Non-WHs (10.4%) ≈ WHs (9.9%), 1995–1998.	Age, sex, patient insurance, and physician specialty	Lack of association in all time periods (1989–1991, 1992–1994, 1995–1998) persisted.
Dominick <i>et al.</i> ³¹	ACE: AAs (31.9%) ≈ WHs (29.2%)	Age, sex, service connection, and having arthroplasty (5 years)	Lack of association persisted
Dominick <i>et al.</i> ³⁰	ACE: AAs (18.0%) ≈ WHs (19.9%)	Age, gender, education, WOMAC, years with OA, and number of affected joints	Lack of association persisted
Yang <i>et al.</i> ³⁹	ACE: AAs (17.9%) > WHs (9.5%) COR: AAs (4.1%) ≈ WHs (2.4%) HYA: AAs (0.6%) ≈ WHs (1.3%)	Unadjusted	N/A
Lapane <i>et al.</i> ⁴¹	COR and HYA: AAs less likely than WHs to report use	Age, gender, income, radiographic severity, history of knee injury, WOMAC, quality of life, acetaminophen use, and chondroitin use	Race difference persisted
Kingsbury <i>et al.</i> ⁴⁰	ACE: Non-WHs (18.2%) > WHs (11.6%)	Unadjusted	N/A
Abbate <i>et al.</i> ⁴³	COR/HYA: Non-WH race not associated with intra-articular injection use (multivariable-adjusted model)	Age, sex, income, health, body mass index, WOMAC, OA symptoms, and knee/hip OA	Lack of associations persisted
Wu <i>et al.</i> ³³	COR: Knee injection, AAs (31.5%) & HISs (26.5%) < WHs (34.0%). Hip injection, AAs (14.5%) ≈ HISs (11.9%) ≈ WHs (15.0%).	Gender, age, substance use, medical insurance, rural/urban, and income	Race difference (in knee injection) and lack of association (in hip injection) persisted

AA, African-American; ACE, Acetaminophen; COR, Corticosteroid joint injection; HIS, Hispanic; HYA, Hyaluronic acid joint injection; OA, osteoarthritis; WH, White; WOMAC, Western Ontario and McMaster Universities Osteoarthritis Index.

sisted despite adjustment for patient sociodemographic and clinical characteristics.

All four studies that investigated the use of herbal products for OA found that AAs and WHs were equally likely to report use of these products (Table 5).^{39,44,45,48} Katz and Lee's⁴⁵ study also found no difference in the use of herbal products

between HISs and WHs. In contrast, the New Mexico study found that HISs were twice as likely as WHs to report use of herbal products for OA and other musculoskeletal diseases.⁴⁷

Discussion

NSAIDs are the mainstay of the pharmacologic management of OA of the knee, hip, and several

Table 5. Studies that investigated race/ethnic differences in the use of complementary and alternative medicines (CAMs) for OA.

Investigator(s)	Findings	Variables adjusted for	Findings after adjustment
Coulton <i>et al.</i> ³⁴	VIT: AAs (5%) ≈ HISs (5%) ≈ WHs (5%)	Unadjusted (for VIT)	N/A
Mikulskis <i>et al.</i> ⁴⁴	GLU/CHO: AAs (7%) < WHs (18%) HER: AAs (~<20%) ≈ WHs (~<20%)	Age, gender, education, and joint swelling (for use of any CAM therapy)	Any CAM therapy: No race association
Herman <i>et al.</i> ⁴⁷	GLU: HISs (15.4%) < WHs (34.1%) CHO: HISs (11.2%) < WHs (24.0%) HER: HISs (14.0%) > WHs (6.6%) MIN/VIT: HISs (12.4%) ≈ WHs (11.8%)	Age, sex, education, income, duration of disease, disability, pain, arthritis helplessness, and medical skepticism	General patterns of ethnic differences similar but statistical significant effects somewhat different
Katz and Lee ⁴⁵	GLU/CHO: AAs (10.7%) ≈ HISs (9.8%) ≈ WHs (14.6%) HER: AAs (6.5%) ≈ HISs (6.0%) ≈ WHs (5.5%) MIN/VIT: AAs (17.4%), HISS (15.9%) > WHs (11.9%)	Sex, age, body mass index, pain severity, WOMAC function, WOMAC stiffness, and patient's global assessment (for use of any CAM therapy)	Any CAM therapy: HISs < AAs and WHs < AAs
Albert <i>et al.</i> ³⁶	MIN/VIT: AAs (19.4–42.6%) < WHs (30.9–45.7%)	Gender and severity of arthritis (stratified only)	N/A
Yang <i>et al.</i> ³⁹	GLU: AAs (11.6%) < WHs (31.7%) CHO: AAs (10.4%) < WHs (29.0%) HER: AAs (3.0%) ≈ WHs (1.2%) MIN/VIT: AAs (5.5%) ≈ WHs (6.4%)	Unadjusted	N/A
Kingsbury <i>et al.</i> ⁴⁰	GLU/CHO: Non-WHs (24.5%) < WHs (47.4%)	Unadjusted	N/A
Vina <i>et al.</i> ⁴⁸	GLU/CHO: AAs (9.8–11.7%) < WHs (14.3–20.7%) HER: AAs (11.4–33.8%) ≈ WHs (14.7–19.1%) MIN/VIT: AAs (46.6–54.6%) ≈ WHs (50.8–53.8%)	Recruitment site, age, WOMAC total, and comorbidities	Race difference in GLU/CHO use persisted. Lack of association in HER, and MIN/VIT use persisted

AA, African-American; CAM, complementary and alternative medicines; CHO, chondroitin; GLU, glucosamine; HER, herbals; HIS, Hispanic; MIN, minerals; VIT, vitamins; WH, White; WOMAC, Western Ontario and McMaster Universities Osteoarthritis Index.

other joints.⁴⁹ Their use is endorsed by the ACR and the AF and OARSI.^{10,11} Although there are potential adverse effects (e.g. gastrointestinal bleeding and renal insufficiency), NSAIDs are the most commonly used pharmacologic treatment for OA.⁴⁹ We found greater use of non-selective NSAIDs among AAs and HiSs than among WHs in several studies.^{28,31,32,38–40} Race difference was not found in other studies^{30,43} with

relatively smaller sample sizes that are susceptible to selection bias. While this class of medication may be beneficial for OA, vigilance for potential side effects affecting NSAID users would be appropriate. While non-selective and COX-2-selective NSAIDs have similar efficacy as analgesic and anti-inflammatory agents, COX-2-selective NSAIDs may be a better option in some due to reduced risk of certain toxicities (e.g.

gastrointestinal toxicity) and the presence of comorbidities. We found less use of this type of NSAIDs among AAs compared to WHs in a few studies,^{31,32,39,40} which was consistent with Reyes and Katz's¹⁷ findings. Clinicians may consider prescription of COX-2-selective over non-selective NSAIDs if appropriate upon choosing the best therapy for AA patients with OA.

In the last few decades, opioids have been increasingly used in the United States and worldwide to treat chronic pain conditions.^{50,51} Chronic use of opioids has been associated with increased risk for fractures, cardiovascular events, and greater mortality.⁵² Other adverse effects include opioid dependence and overdose.⁵³ The ACR and the AF conditionally recommend against their use (except for tramadol) in patients with knee and/or hip OA.¹⁰ However, these organizations also acknowledge that the use of opioids may be appropriate under certain circumstances (e.g. other therapies are contraindicated) and when the benefits of use greatly outweigh the risks of use. Most OA studies found no race/ethnic differences in the use of opioids,^{30,36,39,40,42-44} but a few found less opioid prescription receipt among AAs compared to WHs.^{29,31} Reyes and Katz's¹⁷ review concluded that WH patients were generally more likely than AA and HIS patient to receive an opioid prescription. Constant evaluation of the appropriateness of the long-term use of opioids in all OA patients would be prudent.

Acetaminophen/paracetamol is often the initial therapy for mild OA because it is inexpensive, relatively safe, and effective.⁵⁴ Its use is also recommended by the ACR and the AF, and OARSI.^{10,11} Hepatotoxicity is a rare side effect, except when used in high dosages with concurrent alcohol abuse or with other hepatotoxic medications. Evidence suggests that acetaminophen/paracetamol may be less effective than NSAIDs in OA patients with moderate to severe levels of pain.⁵⁴ We discovered that most studies found no race differences in the use of acetaminophen among those with OA.^{28,30,31} A few studies that used OAI data found that acetaminophen was more commonly used by racial minorities than WHs, however.^{39,40} Regardless, acetaminophen/paracetamol would be a good first-line agent among those with mild-to-moderate OA symptoms.

Intra-articular glucocorticoid injections can reduce knee OA-related pain short term.⁵⁵ Despite controversy as to whether its use may result in cartilage

volume loss in the knee,⁵⁶ intra-articular glucocorticoid injection use is still recommended for use in knee and hip OA by professional organizations.^{10,11} A meta-analysis that included 89 clinical trials showed that intra-articular hyaluronic acid injection is associated with a small and clinically irrelevant benefit and with an increased risk for adverse events.⁵⁷ The OARSI conditionally recommends its use for knee OA, but the ACR and the AF recommend against its use for knee and hip OA.^{10,11} Among the few studies that investigated potential race differences in the use of intra-articular therapies for OA, no appreciable differences were observed.^{39,43} Two studies, however, found that AAs were less likely than WHs to receive either glucocorticoid or hyaluronic joint injection upon evaluating certain subsets of OA patients (e.g. only those who had received any joint injection ever).^{33,41}

While CAMs are very popular, there is limited support of their efficacy in OA treatment from clinical trials.^{10,11} A recent systematic review and meta-analysis of dietary supplements for OA, for instance, found that the quality of evidence for their efficacy was low.⁵⁸ Glucosamine and chondroitin, in particular, were found to be ineffective or to have showed statistically significant but clinically unimportant treatment effects.⁵⁸ The ACR and the AF recommend against the use of joint health supplements in patients with knee and hip OA.¹⁰ Chondroitin sulfate is conditionally recommended for those with hand OA based on a single clinical trial. We found that most studies observed less use of joint health supplements among racial/ethnic minorities compared to non-Hispanic WHs.^{39,40,44,47,48} Clinicians should consider discussing with patients who use these supplements whether medication continuation would be appropriate, especially given their cost. While the ACR and the AF also do not recommend use of vitamin D for any type of OA, there were no specific recommendations regarding the use of other vitamins and minerals for OA.¹⁰ More studies are also recommended to determine the treatment effect of other CAMs, including herbal products.¹⁰ In general, minimal to no racial/ethnic differences in the use of vitamins, minerals, and herbal products were observed by most OA studies.^{34,39,44,45,47,48} Katz and Lee's⁴⁵ finding of race and ethnic differences in the use of vitamins or minerals could be related to the fact that they evaluated clinical trial participants instead of general community members. Clinical trial participants can have very different characteristics from the general population. Reyes and Katz's¹⁷ literature review concluded

that racial/ethnic minorities may rely more on alternative therapies and did not provide details on specific CAM therapies.

Many studies that we examined re-evaluated observed racial and ethnic differences in the use of these OA therapies after adjustment for various sociodemographic and clinical characteristics. Indeed, various sociodemographic (e.g. age, gender, and income) and clinical (e.g. OA disease severity and comorbidities) factors may act as mediators or may partially mediate the relationship between race/ethnicity and OA treatment use.⁵⁹ A few studies found that observed racial/ethnic differences in the use of conventional and CAM therapies for OA were no longer significant when adjusted for these variables,^{27,32,38,44} suggesting that differences in sociodemographic and clinical factors could at least partially explain the observed differences in pharmacologic OA treatment use. However, several other studies that observed racial/ethnic differences in the use of NSAIDs,^{28,31,32,36} opioids,^{29,31} joint injections,^{33,41} and CAM therapies^{45,48} found that the differences persisted after adjustment for these variables. These particular studies suggest that other unmeasured or unobserved variable/s could be the cause of observed racial/ethnic differences in OA treatment use. Several patient-level (e.g. treatment preferences), healthcare systems-level (e.g. availability of translation services and organizational changes in healthcare delivery), and care process-level (e.g. implicit bias and stereotyping) factors are often difficult to measure but could potentially mediate racial/ethnic differences in treatment use.⁶⁰

Study limitations

This literature review has a few limitations. First, we found no studies that examined race/ethnic difference in the use of a few of the pharmacotherapies used in treating OA, such as tramadol and duloxetine. Tramadol is a weak opioid agent conditionally recommended for knee/hip OA treatment.¹⁰ It is particularly recommended when patients have contraindications to NSAIDs or if they find other therapies ineffective. Similarly, evidence suggests that duloxetine has efficacy in OA and is also recommended for use in OA.¹⁰ This agent works through the central nervous system but is not commonly used for OA. Second, we found only two studies that compared the use of OA therapies between Asian Americans and WHs. In Katz and Lee's⁴⁵ investigation, 83% of Asian Americans compared to 89% of WHs

reported use of any CAM therapy for OA. In Wu *et al.*'s³³ investigation, Asians may be less likely than WHs (28.7% *vs* 34.0%) to receive a knee injection for OA. The dearth of studies on use of OA treatments by Asians is likely due to the small number of Asian Americans represented and recruited. Third, we found no study outside the United States that examined racial/ethnic differences in the use of OA pharmacologic therapies. Finally, there are also known race differences in the use of joint replacement surgery⁶¹ that can affect race differences in OA-related pain and disease severity. This review was focused on differences in pharmacologic treatments for OA. Future reviews should examine the evidence related to race and ethnic differences in the surgical management of OA and how they may affect race differences in the pharmacologic management of OA.

Summary

Racial and ethnic differences exist in the utilization of pharmacologic treatments for OA. AAs and HISs are more likely to receive a prescription and to be using prescription oral non-selective NSAIDs than non-Hispanic WHs. In contrast, AAs are less likely than WHs to have a prescription for COX-2-selective NSAIDs. There appears to be minimal race and ethnic differences in the patient-reported use of opioids for OA. AAs and WHs are also equally likely to use or receive other conventional therapies for OA, including acetaminophen and intra-articular therapies. However, there is limited evidence to suggest that AAs may be less likely than WHs to receive opioid and intra-articular injection among certain subsets of OA patients. AAs are also less likely than WHs to report using joint health supplements. There are minimal differences in the use of vitamins, minerals, and herbal products between the two racial groups. Future studies should identify modifiable factors that could help minimize race and ethnic differences in the utilization of evidence-based OA treatments.

Ethics approval and consent to participate

Our study did not require ethical board approval because it is a review of the literature.

Consent for publication

Not applicable.

Author contribution(s)

Ernest R. Vina: Conceptualization; Data curation; Formal analysis; Investigation; Methodology;

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Availability of data and materials

Data are available upon reasonable request.

Supplemental material

Supplemental material for this article is available online.

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